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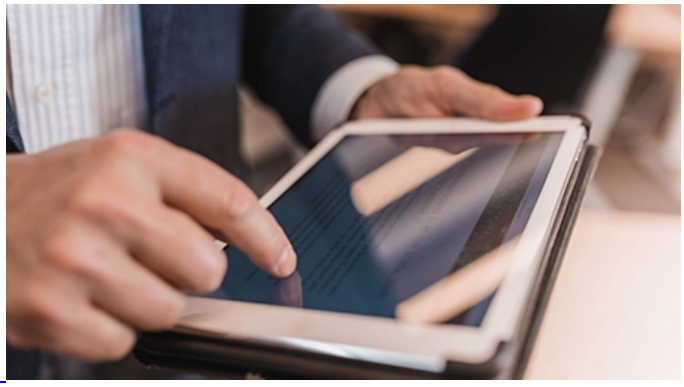

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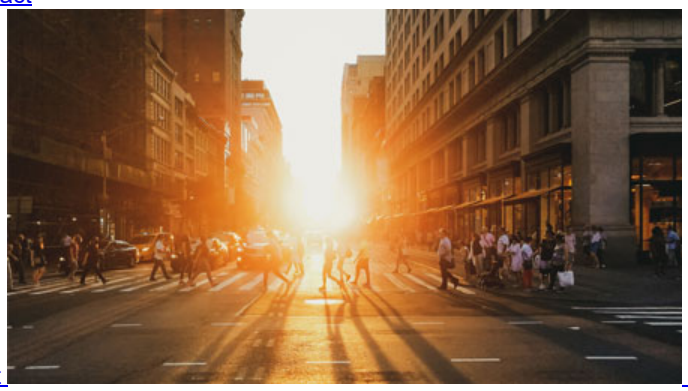

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Evusheld long-acting antibody combination approved in the EU for the treatment of COVID-19

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Evusheld significantly reduced risk of severe COVID-19 or death in TACKLE Phase III treatment trial

AstraZeneca's *Evusheld* (tixagevimab and cilgavimab, formerly AZD7442), a long-acting antibody combination, has been approved in the European Union (EU) for the treatment of adults and adolescents (aged 12 years and older weighing at least 40 kg) with COVID-19 who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19.

The approval by the European Commission was based on results from the TACKLE Phase III COVID-19 treatment trial which showed one intramuscular (IM) dose of *Evusheld* provided clinically and statistically significant protection against progression to severe COVID-19 or death from any cause compared to placebo. *Evusheld* treatment earlier in the disease course led to more favourable outcomes. TACKLE was conducted in non-hospitalised adults with mild-to-moderate COVID-19 who were symptomatic for seven days or less. 90% of trial participants were at high risk of progression to severe COVID-19 due to co-morbidities or age. *Evusheld* was generally well tolerated in the trial.[1]

Michel Goldman, M.D., Ph.D., Professor, Institute for Interdisciplinary Innovation in Healthcare, Université Libre de Bruxelles, and former Executive Director of the European Innovative Medicines Initiative, said: “Many people, including those who are immunocompromised, older adults and those with underlying health conditions, are at high risk of severe disease, hospitalisation and death if they become infected. *Evusheld*, delivered in a convenient intramuscular formulation, is now a much-needed new COVID-19 treatment option for these vulnerable populations.”

Iskra Reic, Executive Vice President, Vaccines and Immune Therapies, AstraZeneca, said: “COVID-19 remains an ongoing health concern for millions of Europeans and around the world, especially for those who may not be well-protected against the virus from vaccination. With this approval, *Evusheld* is now the only long-acting antibody combination available for both prevention and treatment of COVID-19 in Europe, allowing us to protect even more people from this devastating disease.”

The recommended dose of *Evusheld* for treatment in Europe is 300mg of tixagevimab and 300mg of cilgavimab, administered as two separate, sequential IM injections.

Evusheld has been shown to retain *in vitro* neutralisation of Omicron BA.5, which is currently the dominant SARS-CoV-2 variant in Europe.[2] Real-world evidence generated to date has demonstrated significantly lower rates of symptomatic COVID-19 and/or hospitalisation/death for immunocompromised patients receiving *Evusheld* compared to control arms. This includes real-world evidence collected while Omicron BA.5, BA.4, BA.2, BA.1 and BA.1.1 were circulating.[3-6]

Evusheld was granted marketing authorisation in the EU for pre-exposure prophylaxis (prevention) of COVID-19 in a broad population of adults and adolescents earlier this year and is already available in a majority of countries in Europe.

Notes

TACKLE
TACKLE is a Phase III, randomised, double-blind, placebo-controlled, multi-centre trial assessing the safety and efficacy of a single 600mg IM dose of *Evusheld* (300mg each of cilgavimab and tixagevimab) compared to placebo for the treatment of mild-to-moderate COVID-19. The trial was conducted in 95 sites in the US, Latin America, Europe and Japan. 903 participants were randomised (1:1) to receive either *Evusheld* (n = 452) or saline placebo (n = 451), administered in two separate, sequential IM injections.

Participants were adults 18 years-old and over who had mild-to-moderate COVID-19 and were symptomatic for seven days or less. Participants had a documented laboratory-confirmed SARS-CoV-2 infection, as determined by a molecular test (antigen or nucleic acid) from any respiratory tract specimen (e.g. oropharyngeal, nasopharyngeal, or nasal swab or saliva) collected no more than three days prior to day 1. Participants were not vaccinated against COVID-19 at the time of screening.

Detailed results from TACKLE, published in *The Lancet Respiratory Medicine*, showed *Evusheld* significantly reduced the relative risk of progressing to severe COVID-19 or death (from any cause) by 50% (95% confidence interval [CI] 15, 71; p=0.010) through day 29 compared to placebo in non-hospitalised patients with mild-to-moderate COVID-19 who were symptomatic for seven days or less, the trial’s primary endpoint. In pre-specified analyses of participants who received treatment within three days of symptom onset, *Evusheld* reduced the risk of developing severe COVID-19 or death (from any cause) by 88% compared to placebo (95%

CI 9, 98), and the risk reduction was 67% (95% CI 31, 84) compared with placebo when participants received *Evusheld* within five days of symptom onset.[1]

Evusheld was generally well tolerated in the trial. Adverse events (AEs) occurred more frequently in the placebo group (163/451; 36%) than the *Evusheld* group (132/452; 29%). The most common AE was COVID-19 pneumonia, occurring in 49 participants (11%) in the placebo group and 26 participants (6%) in the *Evusheld* group. Serious AEs occurred in 54 participants (12%) in the placebo group and 33 participants (7%) in the *Evusheld* group. There were six COVID-19-reported deaths in the placebo group and three in the *Evusheld* group.[1]

Evusheld
Evusheld, formerly known as AZD7442, is a combination of two long-acting antibodies - tixagevimab (AZD8895) and cilgavimab (AZD1061) - derived from B-cells donated by convalescent patients after SARS-CoV-2 infection. Discovered by Vanderbilt University Medical Center and licensed to AstraZeneca in June 2020, the human monoclonal antibodies bind to distinct sites on the SARS-CoV-2 spike protein[7] and were optimised by AstraZeneca with half-life extension and reduction of Fc effector function and complement C1q binding.[8] The half-life extension more than triples the durability of its action compared to conventional antibodies;[9-11] data from the PROVENT Phase III trial show protection lasting six months.[12] The reduced Fc effector function aims to minimise the risk of antibody-dependent enhancement of disease - a phenomenon in which virus-specific antibodies promote, rather than inhibit, infection and/or disease.[13]

Evusheld is authorised for use for pre-exposure prophylaxis (prevention) of COVID-19 in the US (emergency use), EU, Japan and many other countries. *Evusheld* is approved for treatment of those with risk factors for severe SARS-CoV-2 infection in Japan. Regulatory submissions are progressing for both prevention and treatment indications around the world.

Evusheld is being developed with support from the US government, including federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority in partnership with the Department of Defense; Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense, under Contract No. W911QY-21-9-0001.

Under the terms of the licensing agreement with Vanderbilt, AstraZeneca will pay single-digit royalties on future net sales.

AstraZeneca
AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Twitter @AstraZeneca.

Contacts

For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

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